MECHANICAL MODELING OF SINGLE CELL-EXTRACELLULAR MATRIX COUPLING

Tommy Heck, Tim Odenthal, Bart Smeets, Paul van Liedekerke, Herman Ramon and Hans Van Oosterwyck

Introduction

Cell migration, which is a vital process for tissue maintenance and development, consists of multiple integrated steps: front-to-back polarization, membrane extension by actin polymerization-driven protrusion and adhesion formation, translocation of the cell body and retraction of the rear. In order to migrate, cells must apply forces to the extracellular matrix (ECM) and degrade it in a coordinated fashion. At the same time, these forces regulate the formation and stability of adhesions and remodeling of the actin cytoskeleton by a process called mechanotransduction. Since formation of adhesions between the cell and the ECM and application of forces to the ECM are important in cell migration, a mechanically relevant cell-ECM coupling is required in computational cell migration models. Here, we aim to couple a cell model to a deformable and degradable model of the ECM to investigate the effects of mechanical properties and susceptibility to proteolytic degradation of the ECM on cell migration.

Methods

A deformable cell model, developed earlier for studying initial cell spreading, is used [1]. In the model, the membrane and actin cortex of the cell are discretized into deformable rounded triangles, allowing a mechanically correct calculation of contact forces between the cell and the ECM. The deformable cell model will be embedded in a 3D polyethylene glycol (PEG) gel, which will be modeled by smoothed particle hydrodynamics (SPH). PEG is a hydrogel that can be assumed continuous at the cellular level and has tunable physical (e.g. adhesive ligand and proteolytic degradable peptides) and mechanical properties. SPH is a meshless Langrangian numerical method in which a material is represented by a set of discrete elements, called particles, which represent a finite mass of the material and carry physical variables (e.g. density and velocity). Continuous laws from fluid and solid mechanics can be implemented in a discrete way, allowing to describe viscoelastic behavior. Due to its meshless character SPH can handle large deformations of the gel and can capture cell migration through the gel in a natural way, in contrast to mesh-based methods as the finite element method (FEM) where frequent remeshing would be required.

Results and discussion

As a first step, we have investigated the capability of SPH to capture the mechanical properties of the PEG gel by comparing SPH with FEM. Point forces, representing force transmission through focal adhesions, are applied to a square 2D elastic gel which is constrained at its boundaries. SPH simulations show a similar strain pattern for both x- and y-direction as was observed in FEM simulations, demonstrating that SPH is capable of capturing ECM mechanics (Figure 1). In the near future, the deformable cell and SPH will be coupled to allow simulation of single cell migration through a PEG gel. The effects of stiffness and susceptibility to proteolytic degradation of the PEG gel on migration velocity will be investigated and compared to observations from literature.

References

[1] Odenthal, T et al., *PLoS Comput. Biol.* **9**(10), e1003267, 2013

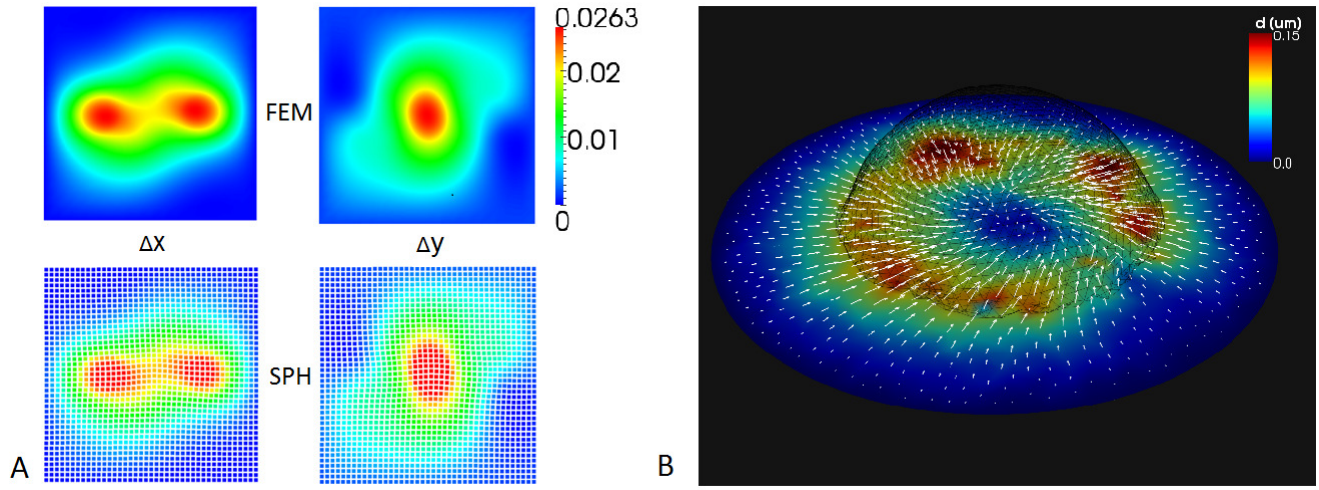

Figure 1: A: deformation in x- (left) and y-direction (right) normalized to the length of the gel after application of point forces simulated with FEM (top) and SPH (bottom) to a square gel. B: 2D substrate deformation due to cell spreading-induced contact forces.